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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,062	01/25/2006	Ni Yicheng	50304/111001	2018

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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
01/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/595,062	YICHENG ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-34* is/are pending in the application.

4a) Of the above claim(s) *17-20 and 25-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16,21-24 and 30-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

This application contains claims directed to the following patentably distinct species: (1) a phenanthro[1,10,9,8-opqra]perylene-7,14-dione compound and (2) an imaging material. The species are independent or distinct because claims to the different species recite the mutually exclusive characteristics of such species. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, the claims are generic.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a

claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

During a telephone conversation with Tiffany Reiter on 12/19/08 a provisional election was made to prosecute the following species: **hypericin** as a phenanthro[1,10,9,8-opqra]perylene-7,14-dione compound (claim 16), and

radionuclide as an imaging material (claim 21). Affirmation of this election must be made by applicant in replying to this Office action. Accordingly claims 15, 16, 21-24 and 30-34 are readable on the elected species. Claims 17-20 and 25-29 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Status of Claims

Claims 15-34 are pending, of which claims 17-20 and 25-29 are withdrawn from consideration at this time as being drawn to non-elected species. Claims 15, 16, 21-24 and 30-34 are readable upon the elected invention and are examined herein on the merits for patentability.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 16, 21-24 and 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention. The claims are rejected as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: performing an imaging procedure. In the instant case, the only active step in the claimed method is administering the compound. However, for the claimed method of "obtaining an image of ischemic, infarcted or necrotic tissue in a subject," an imaging step must be performed in addition to the administration of an imaging agent, therefore the claims are incomplete for omitting essential steps.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is drawn to a method for obtaining an image of ischemic, infracted or necrotic tissue in a subject, comprising the step of administering an imaging agnet comprising an imaging agent comprising a phenanthro[1,10,9,8-opqra]perylene-7,14-dione compound, wherein said compound is hypericin, pseudohypericin or a derivative thereof. The claims are unclear as to the identity of compounds which are within the scope of "a *derivative* thereof." For example, there is no direction provided to describe which out of an almost unlimited number of potential chemical substituents and in what positions on the compound substituents may appear to indicate in which way the compound is to be derivatized. Furthermore, the broadest reasonable interpretation of derivatives of a compound covers all future improvements without regard to whether Applicants invented such improvements, which would

undermine the function of the claims because it would allow Applicants to benefit from the ambiguity, rather than requiring Applicants to give proper notice of the scope of the claims to competitors. Additionally, adopting the broadest reasonable construction of the claims could retard innovation because cautious competitors may steer too far around that which Applicants actually invented, neglecting improvements that otherwise might be made. See *Halliburton Energy Services Inc. v. M-I LLC*, 85 USPQ2d 1654 (Fed. Cir. 2008). Accordingly, the metes and bounds of the claims are not clearly set forth and the scope of the invention cannot be distinctly ascertained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Lavie *et al.* (US 4,898,891).

Lavie discloses topical antiviral pharmaceutical compositions comprising a pharmaceutically acceptable excipient suitable to place the composition into form for topical administration and, as active ingredient, an antiviral effective quantity of a pure compound selected from the group consisting of hypericin, pseudohypericin, a pharmaceutically acceptable salt of hypericin or pseudohypericin, and mixtures thereof (see claim 1).

Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipate by Obermuller *et al.* (*Photochem. Photobiol.,* 2001, 74(2), p. 211-215).

Obermuller discloses optimized hypericin derivatives as photodynamic therapy agents, including a heavy atom-substituted derivative 2,5-diiodo-hypericin (see abstract, Figure on left column of page 213). Heavy-atom substitution, *e.g.* by iodine, of hypericin at the ring sites provides a good means to enhance the desired photosensitized singlet oxygen/superoxide radical formation (page 215).

Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Hudson *et al.* (*Photochem. Photobiol.*, 1999, 70(5), p. 820-822).

Hudson discloses bromohypericins as potent photoactive antiviral agents. See compounds, Table 2, and various solutions; page 820, right column and 822, left column.

Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Stock *et al.* (Stock *et al.*, *Planta Medica*, 1991, 57 Supplement 2, A61) (title).

Stock discloses pharmacokinetic tests using [14C]-labelled hypericin and pseudohypericin (see title).

Claims 15, 16, 30, 31 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Blank *et al.* (*Photochem. Photobiol.*, 2002, 76(3), p. 335-340).

Blank discloses photodynamic therapy using hypericin (page 335). The *in vivo* procedure included **intraperitoneal administration of HY** (5 mg/kg) into mice bearing C26-derived tumors (10–12 mm in diameter). Six hours after administration the animals were anesthetized, and the dorsa of the mice were depilated. The mice were covered with aluminum foil, exposing the tumor and a concentric 2 mm adjacent area. The tumors were irradiated with 550 or 590 nm. Twenty-four hours after the treatment the mice were injected i.p. with 0.4 mL 1% Evans Blue (EB) for **examination** of viable or **necrotic tissues**.

The only active step in the instantly claimed methods includes the administration of hypericin. Therefore, Blanks meets the instant claim limitations, wherein visualization of necrotic tissue in a subject is achieved comprising "administering hypericin."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 15, 16, 21-24 and 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blank *et al.* (*Photochem. Photobiol.*, 2002, 76(3), p. 335-340), in view of Huyghe *et al.* (J. Nuclear Medicine, 2003, 44(5) Supp., p. 303P).

Blank discloses photodynamic therapy using hypericin, including necrosis of tumor, as set forth above. Blanks does not specifically recite that a radionuclide is conjugated to conjugate to hypericin for use in a method of obtaining an image of ischemic, infracted or necrotic tissue in a subject. It is for this reason that Huyghe is joined.

Huyghe discloses that hypericin is an outstanding tool for fluorescence detection of urothelial carcinoma, as well has affinity for non-bladder malignant tissue, and is useful in photodynamic therapy. Radiolabelled hypericin derivatives could be useful for scintigraphic detection and treatment of tumors that are not easily accessible to fluorescence detection or photodynamic therapy. Mono[^{125}I]-iodohypericin was prepared and investigated, and it was determined that ^{123}I-hyp is a potential radiopharmaceutical for in vivo tumor visualization.

It would have been obvious to one of ordinary skill in the art at the time of the invention to provide ^{123}I-hyp, as disclosed by Huyghe, for imaging necrotic tissue produced upon photodynamic therapy using hypericin in the methods of Blank. One would have been motivated to do so, and would have had a reasonable expectation of success in doing so, because Blank teaches that tumor necrosis is achieved upon PDT

therapy using hypericin, and because Huyghe specifically teaches radiolabelled hypericin derivatives to be useful for scintigraphic detection and treatment of tumors that are not easily accessible to fluorescence detection or photodynamic therapy, e.g. in vivo tumor visualization.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS